REMARKS

Claims 1-20, 34, 36-44 and 46-47 are present in this application. Claims 6-8, 11-18, 20, 38-89 and 41-44 are currently withdrawn while claims 1-5, 9-10, 19, 34, 36-37, 40 and 46-47 are under active consideration.

Claims 1-5, 9-10, 19, 34, 36-37, 40 and 46-47 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The office action states that the specification does not provide a sufficient description of a polypeptide with a charged residue. Applicant traverses this rejection.

The applicant is well aware of the requirements for adequate section 112 disclosure, but there is no issue here with a chemical genus and species. Claim 1 recites a charged residue which is exactly what the Lys group is. This language also excludes other residues that are not described in the specification, such as non-charged residues that do not perform as noted in the invention. The skilled artisan knows what similar or equivalent groups can be used instead of Lys, and for these reasons the disclosure is more than sufficient. Furthermore, it is improper to try to restrict applicant's invention to the most preferred embodiment. Also, the rejection does not apply to claims 3-5, 9-10, 19, 34, 36-37, 40 and 46 since those claims are directed to an invention where Lys is present in position 44. In view of these comments, this rejection has been overcome and should be withdrawn.

Claims 1-5, 9-10, 19, 34, 36-37, 40 and 46-47 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, claim 1 was rejected because of the recitation of "without induced mutations or modifications in the original VH/VL interface framework" with the office action alleging that the original residue was Gly rather than Lys.

Applicant traverses this rejection. As the native clone used for exemplifying the invention had a Lys residue at position 44, and not a Gly residue, there is no artificial mutation or modification made to the clone (page 5 second paragraph). This recitation was added to claim 1 to further distinguish the invention from the cited art (see: last paragraph of specification page 3, second and third paragraphs of specification page 9). Thus, the claim language is correct and is not indefinite. Again, the rejection does not apply to claims 3-5,

9-10, 19, 34, 36-37, 40 and 46 since those claims are directed to an invention where Lys still remains present in position 44. Accordingly, this rejection should also be withdrawn.

Claims 1-5, 9-10, 19, 34, 36-37, 40 and 46-47 were again rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. The reason for this rejection appears to be based on a typographical error in the specification where the term "we" was mentioned in connection with the conducting of various experiments. Although that term was used to refer to the team that conducted the experiments, this has now been changed so that there can be no confusion as to whether additional inventors participated, which they did not. No new matter has been introduced, so that these changes should be entered. Those errors have now been corrected by amendment and, as a certified copy of an English language priority document is of record, the subsequently published Reiter document is not an effective prior art reference and no rejections can be made based on it. For these reasons, this rejection should be withdrawn.

Claims 1-5, 9-10, 19, 34, 36-37, 40 and 46-47 were rejected under 35 U.S.C. 103(a) as being unpatentable over del Rio et al. EP 712,863 ("del Rio") in view of the de Wildt article. The Examiner acknowledges that del Rio does not disclose a polypeptide having a charged residue at position 44 but alleges that de Wildt discloses that heavy chain with Lys residue has the highest affinity to an antigen so that it would be obvious to place a charged residue at position 44. Applicant respectfully traverses this rejection.

Applicant submits that it would not been obvious to replace the Gly residue with Lys residue in position 44 of the framework since according to the present invention this does not result in increased affinity as found by de Wildt but in increased stability. De Wildt discloses that the contribution of the Lys residue in CDR3 to specific binding but does not mention or suggest Lys or other charged residues in the framework. All the antibody fragments according to the present invention have a charged residue such as Lys at position 44 of the framework, but only selected ones, with the specific CDR3 sequence, bind antigens of interest. Therefore, the advantage taught by de Wildt for increasing affinity by having Lys residue within the CDR3 sequence would not provide any motivation to increase stability by replacing position 44 of the VH/VL interface framework with a Lys residue. Thus, the skilled artisan would not be led to substitute the Lys residue into the framework as taught by the present invention, so that this rejection should be withdrawn.

Finally, as noted above, a petition to extend the time for responding is enclosed.

In view of the above, the entire application is believed to be in condition for allowance, early notice of which would be appreciated. Should any issues remain, a personal or telephonic interview is respectfully requested to discuss the same in order to expedite the allowance of all the claims in this application.

Respectfully submitted,

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